PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

10/510147

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
57767WO004		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 03/10285	01.04.2003	05.04.2002
International Patent Classification (IPC) or both national classification and IPC		
A61K9/12, A61K9/12		
Applicant		
3M INNOVATIVE PROPERTIES COMPANY et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.10.2003	04.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Luangkhot, N Telephone No. +49 89 2399-7857

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/10285

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-22 as originally filed

Claims, Numbers

1-15 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) The documents cited in the International Search Report (ISR) were numbered respectively from D1-D5; this numbering results from the citation order in the ISR and will be used for the procedure. Unless otherwise specified, the **cited passages of each document in the ISR will be considered.**

2) **Novelty and inventive step according to Art. 33(2) and 33(3) PCT**

2a) Claim 1 and its dependent claims 2-15 are novel because none of the cited documents describe an aerosol formulation comprising formoterol, a compound of formula (I) such as ciclesonide and a propellant selected from HFA 134a, HFA 227 and a mixture thereof.

2b) The subject-matter of present application seems to lack the necessary inventive step for the following reasons:

D1, filed by the same applicant and cited in present application, is directed to a suspension formulation for MDI containing (a) micronized **formoterol**, (b) 0.1%-5.0% w/w ethanol, (c) HFA134a or HFA227 or mixture thereof (d) optionally a micronized bulking agent such as lactose, DL-alanine, ascorbic acid, glucose or trehalose in order to prevent quick-flocculation or sedimentation or caking and (e) optionally a surfactant (see p.5). The formulation of D1 is being characterized in that it exhibits substantially no growth in particle size or change in crystal morphology over a prolonged period, is substantially and readily redispersible and upon redispersion does not flocculate so quickly as to prevent reproducible dosing of the drug. These characteristics are also described in present application.

D2, filed by present applicant and cited in present application, is directed to a solution formulation for MDI containing (a) dissolved **ciclesonide** (b) 3-25% preferably 5-20% preferably 7-12 % ethanol (c) HFA134a or HFA227 or mixture thereof. The formulations of D2 (see example 13-16) show good physical and chemical stability (see p.12 L.5-6, claim 1, p.39). These characteristics are also obtained in present application.

The difference with D1 consists in that the formulation of D1 does not contain

dissolved ciclesonide.
The difference with D2 consists in that D2 does not contain suspended formoterol.

The problem to be solved can be seen as providing a formulation for MDI containing formoterol **and** ciclesonide.

As combination of drugs is a **frequent and common practice** in the field of "drug-delivery to the lungs for the treatment of respiratory disorders" (in particularly combination of a beta-agonist with a glucorticoide) and there is no indication in prior art stipulating that the combination of formoterol and ciclesonide is not feasible, the skilled man in the art does not need to be inventive by combining the teachings of D1 or/and D2 and/or formoterol formulation of D1 with ciclesonide or ciclesonide formulation with formoterol, and thus arrives at the claimed composition of present application with the obtention of the same advantages as described in D1 and D2, or D3 (well-known advantages related to a suspension and a solution ->see p.1 L.23- p.2 L.25).
The set up of the optimal amount of ethanol in order to dissolve ciclesonide but not formoterol is a matter of routine for the skilled man in the art (see also D3 p.6 L.36 and p.7 L.2). Additionally D3 describes a method of preparing an aerosol formulation wherein a **first drug is dissolved** in an ethanol/ HFAs mixture and a **micronized second drug** is added in order to obtain a suspension (see claims or example 1).

As long as applicant does not **providence evidence of a surprising effect,** the claimed composition would be considered as an **obvious** combination that the skilled man in the art wil perform **routinely**.

Therefore in view of the disclosure and teachings of D1-D2 claims 1-15 does not involve an inventive step.

2c) Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply and not be incorporated into the application.

3) Clarity according to Art. 6 PCT

3a) It seems that WO99/28296, cited in present application on p.6 L.18, should not be cited as state of the art because its content, which is directed to a method for producing lactams, seems not to be relevant for present application.

3b) Chemical stability tests were carried for ciclesonide only for an **only 5 days storage.** Applicant's attention is drawn with the fact that examining division doubts that these results regarding chemical stability with a storage of 5 days can be extrapolated to **2 or 3 years** (see present application p.22 L.16-20).

4) The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT). Preferably these indications should be submitted in **handwritten form** on a copy of the relevant parts of the application as filed.